Docket No. 4009379-180240 **PATENT**

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**IN THE UNITED STATES PATENT & TRADEMARK OFFICE**

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| Applicant: | Ulf Gyllensten et al | : | Confirmation No. 2553 |
| Serial No.: | 10/529,447 | : | Group Art Unit: 1637 |
| Filing Date: | December 12, 2005 | : | Examiner: Thomas, David C. |

For: **Method and Kit for Quantitative and Qualitative Determination of Human Papillomavirus**

# REPLY BRIEF

Mail Stop Appeal Brief - Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

The present Reply Brief is submitted in response to the Examiner's Answer dated November 12, 2009.

## I. All the Elements of Claim 9 are Not Taught

At page 16, the Examiner's Answer states that the central 35 U.S.C. 103(a) rejection depends upon whether all of the claim elements are taught by the combination of Kroeger, Gissmann, Goldsborough, Seedorf, Sastre-Garau and Buck and whether there is motivation to combine the references.

However, in the sentence bridging pages 18 and 19, the Examiner's Answer then admits that Gissmann, Goldsborough, Seedorf and Sastre-Garau fail to teach the specific primers or probes of claim 9. Thus, by admission, not all the elements of claim 9 are taught in any of the references. As

the primers and probes of claim 9 are not taught, claim 9 is not rendered obvious by the cited combination of references. Any motivation to combine the teachings of the cited references is irrelevant to the patentability of claim 9.

The Examiner's Answer appears to overlook this significant deficiency by asserting that each of these references teaches a sequence from which one of skill in the art would be able to design a gene-specific primer and probe set for detection of a specific HPV type for a kit. However, the test for patentability is not what one of skill would be able to do. Moreover, the Examiner has not shown that it would have been obvious to so design a gene-specific primer and probe set for detection of a specific HPV type, or to combine the particular primer and probe sets of claims 9 and 21 in a kit as claimed. Accordingly, the rejections of claims 9 and 21 must be reversed.

## II. The Kit of Kroeger Does Not Teach Targeting a Kit for Amplification in Different HPV Reading Frames

In the paragraph bridging pages 19 and 20, the Examiner's Answer admits that the single set of primers and the cocktail of multiple probes of Kroeger target only one gene, L1, but relied on Gissmann, Goldsborough, Seedorf and Sastre-Garau as teaching sequences homologous to the cited HPV genes and asserted one of skill in the art would be able to design a gene-specific primer and probe set for detection of a specific HPV type and combine the sets into a kit.

Appellants again note that the test for patentability is not what one of skill would be able to do. Moreover, notwithstanding the limited homology between the individual teachings of the cited references and the presently disclosed primers and probes, none of Kroeger, Gissmann, Goldsborough, Seedorf and Sastre-Garau teach primers and probes targeting a combination of HPV genes as set forth in claim 21, particularly, comprising forward and reverse E7 amplification primers for HPV 16, forward and reverse E1 amplification primers for HPV 18 and 45, and forward and reverse E6 amplification primers for HPV 31, and probes therefore. Neither the kit of Kroeger, directed to targeting the L1 gene, nor the teachings of Gissmann, Goldsborough, Seedorf and Sastre-

Garau, individually directed to respective genes, teach or suggest a combination of primers and probes targeting the genes as recited in claim 21 in a single kit. Accordingly, the rejection of claim 21 must be reversed.

## III. *In re Kubin* is not Relevant to the Present Issues

Beginning at page 22, the Examiner's Answer asserts that *In re Kubin,* 83 U.S.P.Q.2d 1410 (Bd. Pat. App. & Int. 2007) supports use of the "obvious to try" test for patentability in the present application.

Appellants disagree. In the *Kubin* case, the Board considered the obviousness of a claimed nucleotide sequence encoding natural killer cell activation inducing ligand (NAIL) polypeptide based on a prior art disclosure of the NAIL protein and an express teaching on how to isolate its cDNA by conventional techniques. The Board found there were a limited number of methodologies for isolation of NAIL cDNA and a skilled artisan would have had reason to try these methodologies with reasonable expectation that at least one would be successful. However, in the present application, Kroeger, along with Gissmann, Goldsborough, Seedorf and Sastre-Garau, show there are an almost infinite number of sequences that can be selected from the teachings of the secondary references and an almost infinite number of combinations thereof, with no evidence or expectation that all such sequences allow detection and quantification of different HPV types. Thus, neither the combination of primers and probes of claim 9 nor the combination of primers and probes of claim 21 are selected from a limited number of known possibilities as was the case in *Kubin* where the Board found that "obvious to try" was an acceptable test for obviousness. It is therefore apparent that the facts of the present application are significantly distinguishable from those of *Kubin* and particularly, there is not a limited number of possibilities from which one of ordinary skill in the art can select the claimed combinations. Accordingly, the "obvious to try" test for patentability is not

proper in the present application and does not render the combination of primers and probes of claim 9 nor the combination of primers and probes of claim 21 obvious.

To the contrary, none of the secondary references of Gissmann, Goldsborough, Seedorf or Sastre-Garau are directed to detection and quantification of HPV. Thus, even if the sequences at the various positions noted by the Examiner could be used for detection and quantification, there is no indication in any of the references or otherwise of record which would have motivated one of ordinary skill in the art to select such sequences and employ them in combination. In determining patentability under 35 U.S.C. §103, it is necessary to determine whether there was an apparent reason to combine the known elements in the fashion of the claim at issue, *KSR International Co. v. Teleflex, Inc.*, 550 US 398, 418 (2007). None of the cited references provide any apparent reason to select from the various teachings of each secondary reference the portions of sequences asserted as relevant by the Examiner and to combine such selected teachings as primers and probes in a single kit as recited in claim 9 or claim 21, particularly to provide the ability to analyze multiple types of HPV, or groups of HPV, in one reaction vessel, without competition among the various primers and probes during amplification and detection.

The rejection of claims 9 and 21 should therefore be reversed.

## IV. Buck Does Not Teach Equivalents Known for the Same Purpose

In the paragraph bridging pages 24 and 25, the Examiner's Answer correctly states that to rely on equivalence as a rationale supporting an obviousness rejection, the equivalency must be recognized in the prior art. However, the Examiner's Answer then asserts that Buck's use of a highly pure template for testing primers under optimal screening conditions provides an ordinary practitioner with a reasonable expectation of success for successful amplification of a known sequence in an impure sample after initially identifying candidate primers.

Buck only discloses amplification of a single test nucleic acid and Buck's results were obtained under optimal sequencing conditions with highly pure template and primer and the new generation of sequencing reagents such as the dichlororhodamine dye terminators. The Examiner's Answer provides no reasoning as to how Buck's limited and controlled experimental work demonstrates to one of ordinary skill in that art that all sets of primers and probes which may be derived from the teachings of Gissmann, Goldsborough, Seedorf and Sastre-Garau will amplify a respective specific HPV nucleic acid while, at the same time, not amplifying a different but very similar HPV nucleic acid. Buck simply provides no disclosure or suggestion in this regard and does not resolve the deficiencies of Kroeger, Gissmann, Goldsborough, Seedorf and Sastre-Garau in failing to render the presently claimed kits obvious.

## V. No Prima Facie Case of Obviousness Established

The Examiner's Answer asserts that there is no evidence that the claimed kit provides unexpected or superior results for detection of multiple HPV types relative to the prior art such as Kroeger (see, for example, pages 18 and 24). However, as no prima facie case of obviousness has been established, there is no need to provide any such evidence. That is, as noted above, none of the prior art discloses the primers and probes of claim 9 or a combination of primers and probes targeting the combination of genes as recited in claim 21. Moreover, while the Examiner's Answer and the rejections assert that primers and probes can be derived from the teachings of Gissmann, Goldsborough, Seedorf and Sastre-Garau, no combination of such primers and probes has been identified. Accordingly, the teachings of the prior art are insufficient to establish a prima facie case of obviousness, so that the patentability of the presently claimed kits is apparent without any comparative evidence.

## VI. Conclusions

For the reasons set for the in detail in the Appeal Brief filed July 27, 2009 and above, the kits defined by claims 9-14 and 18-26 are nonobvious over and patentably distinguishable from the combinations of a) Kroeger in view of Gissmann, Goldsborough, Seedorf, Sastre-Garau, and Buck, b) Kroeger in view of Gissmann, Goldsborough, Seedorf, Sastre-Garau, Buck, and Yoo, c) Kroeger in view of Gissmann, Goldsborough, Seedorf, Sastre-Garau, Buck, and Swan, and d) Kroeger in view of Gissmann, Goldsborough, Seedorf, Sastre-Garau, Buck, Yoo and Swan. Accordingly, the rejections under 35 U.S.C. §103(a) should be reversed. Favorable action by the Board is respectfully requested.

Please charge any fee required in connection with this communication to Deposit Account 503915.

Respectfully submitted,

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